

SHORT THESIS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY (PhD)

Examination of soft tissue calcification using OsteoSense staining-based imaging and investigation of the role of endoplasmic reticulum stress in the vascular calcification-enhancing effect of the prolyl hydroxylase inhibitor Daprodustat

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Introduction

Chronic kidney disease (CKD) affects millions of people worldwide and is currently the eighth leading cause of death. Due to increased life expectancy and an aging population, the prevalence of CKD is expected to increase in the coming decades, placing a significant financial burden on the healthcare system. Calcification of the cardiovascular system (large and medium-sized vessels, heart valves) is observed in CKD patients, which significantly contributes to cardiovascular mortality in these patients.

Calcification of the cardiovascular system was previously considered a passive, purely physicochemical process, in which elevated plasma concentrations of phosphate and calcium lead to the deposition of calcium-phosphate salts in soft tissues. The past 25 years have brought breakthroughs in the understanding of the mechanisms of vascular calcification, and it has become clear that the process is cell-mediated and actively regulated.

Animal models of CKD are of great importance for understanding the pathomechanism of CKD and vascular calcification and for identifying potential therapeutic targets. Previously, the primary model of CKD was 5/6 subtotal nephrectomy, an invasive surgical procedure that destroys the kidney. In the past decade, several new CKD models have been developed, including the one in which CKD is induced by an adenine-containing diet.

The adenine-induced CKD model develops interstitial fibrosis, tubular damage, and significant vascular calcification. The advantage of the adenine model is that the development of CKD closely resembles that of renal failure in humans. In vivo imaging techniques are of increasing importance, not only in diagnostics but also in basic research. For example, near-infrared imaging, which has the great advantage of deeper tissue penetration, may be suitable for detecting calcification.

In my work, I investigated the applicability of the hydroxyapatite-specific OsteoSense dye, which was originally developed to study ossification processes, for the detection of soft tissue calcification in an adenine-induced CKD model in C57BL/6 mouse strain. Furthermore, I investigated the role of endoplasmic reticulum stress in the calcification-enhancing effect of the prolyl hydroxylase inhibitor (PHI) Daprodustat (DPD), developed for the treatment of anemia in CKD patients, using the adenine-induced CKD mouse model and in vitro calcification methods.

Aims

1. In order to study CKD-associated soft tissue calcification, our research group wanted to establish a non-invasive CKD mouse model and a sensitive and specific method for detecting calcification. Based on the literature data, we aimed to establish a CKD mouse model induced by adenine and high phosphate diet. Our further goal was to develop a method that would enable us to detect CKD-associated calcification in various soft tissues by using the Osteosense fluorescent dye *in vivo*.
2. In our previous work, our research group demonstrated the calcification-enhancing effect of PHI Daprodustat, used in the treatment of anemia in CKD patients, in an *in vitro* cellular model and in an *in vivo* CKD mouse model. In this regard, we investigated the molecular mechanism of the pro-calcification effect of DPD, within which we aimed to clarify the role of ER stress.

Methods

- During our experiments, we worked with human aortic smooth muscle cells, which were cultured in Dulbecco's Modified Eagle's Medium supplemented with 10% fetal bovine serum, 1% L-glutamine, 1% sodium pyruvate, and 1% antibiotic and antimycotic reagents. The cells were cultured in an incubator at 37 °C in the presence of 5% CO₂.
- Calcification of the cells was detected by ARS staining. At the end of the experiment, the culture medium was removed from the cells cultured in the 96-well plate, washed with phosphate-buffered saline, and then fixed with 4% paraformaldehyde for 20 minutes. After fixation, the cells were washed again with PBS and 2% ARS solution was added to the cells. After 15 minutes, the dye was removed, and the plate was washed with distilled water. The plate was photographed, then 100 µl of hexadecylpyridinium chloride solution (100 mmol/L) was added, which dissolves the bound dye, making the measurement quantifiable. The absorbance of the samples was measured with a microplate reader at a wavelength of 562 nm.
- For osteocalcin measurement, cells were cultured in 6-well plates. At the end of the treatment, the culture medium was removed from the cells, washed with PBS, and 100 µl of ethylenediaminetetraacetic acid (EDTA) (0.5 mol/L, pH 6.9) was added. The osteocalcin concentration was determined from the EDTA supernatant by ELISA according to the protocol.

- To measure the calcium content of the extracellular matrix, cells were cultured in 96-well plates. At the end of the treatment, the culture medium was removed from the cells, washed with PBS, and the extracellular matrix was decalcified with 0.6 mol/L hydrochloric acid for 5 minutes at room temperature. The calcium content of the hydrochloric acid supernatant was determined using the QuantiChrom Calcium Assay kit according to the prescribed protocol. After decalcification, the cells were washed again and then lysed in a buffer containing 0.1% NaOH and 0.1% SDS. The protein concentration of the lysate was determined using the BCA Protein Assay kit and the calcium content was normalized to the protein content.
- The protein expression of the cells was examined by Western blot analysis. The lysates were separated on a 7.5-10% SDS polyacrylamide gel, then blotted onto a nitrocellulose membrane, after blocked with milk powder solution and incubated with the primary antibody overnight at 4 °C. Next day, the membranes were incubated for 1 hour with horseradish peroxidase-conjugated anti-rabbit or anti-mouse secondary antibody, then chemiluminescent Western ECL reagent was used for detection and the result was recorded on X-ray film or digitally.
- In our animal experiments were conducted with a valid permit issued by the Research Ethics Committee of the University of Debrecen. During the experiments, C57BL/6 male (n=24), 8-12 week-old mice were examined. The mice were randomly divided into 2 groups (n=12): control and CKD. The control group received standard rodent chow, while CKD was replaced with a 2-phase adenine-containing diet, during which the mice received a rodent chow containing 0.2% adenine and 0.7% phosphate for 6 weeks, and then from the 7th week, 0.2% adenine and 1.8% phosphate for an additional 3 weeks. The effect of DPD was examined in another experiment, during which 10 week-old C57BL/6 mice (n=30) were divided into three groups: control, CKD, CKD+DPD. CKD was induced by a biphasic adenine and elevated phosphate diet as in the previous experiment. DPD was administered oral daily from week 7 of the experiment as a 1% methylcellulose suspension, while mice not receiving DPD received the same volume of vehicle.
- OsteoSense 750EX dye was used to examine soft tissue calcification in mice. At the end of the experiment, the animals were anesthetized by inhalation of isoflurane, and OsteoSense dye was injected via the retro-orbital venous sinus. Imaging was performed 18 hours after injection.

- Serum urea, creatinine, phosphate and calcium levels were determined from blood samples taken from the mice using the Cobas® c502 automated instrument.
- The organs were fixed in 10% formalin and embedded in paraffin. Then, 4 µm thick sections were cut. The sections were deparaffinized and rehydrated. After that, hematoxylin-eosin, von Kossa, and Alizarin Red S staining were performed.
- Total RNA was isolated from the organs using Tri-reagent. The RNA was transcribed into cDNA using the High-Capacity cDNA Reverse Transcription Kit. The PCR reaction was performed using iTaq™ Universal SYBR® GreenSupermix and the primers listed in the table below. The PCR reaction was performed in the CFX96 Real-Time System.
- GraphPad Prism 8.01 software was used for statistical analyses. Normal distribution was determined using the Shapiro-Wilk test, and p values were determined using parametric tests. Statistically significant differences between two groups were analyzed using the two-tailed Student's t-test, comparisons of more than two groups were analyzed using Tukey's multiple comparison analysis of variance followed by ANOVA, and comparisons of several treatment groups to a single control were analyzed using Dunnett's post-hoc test followed by ANOVA. Values of $p < 0.05$ were considered significant.

Results

1. Use of OsteoSense staining to detect soft tissue calcification in a CKD mouse model

Soft tissue calcification was investigated in an adenine-induced CKD mouse model in 8-week-old male C57BL/6 mice. In addition to determining renal function parameters from plasma, phosphate and calcium were also measured. Plasma phosphate levels in CKD mice were significantly increased compared to CTRL, but no significant difference was observed in calcium levels

Aortas were imaged within 4 hours of sample collection using the IVIS Imaging instrument. OsteoSense signal intensity was significantly higher in the aorta of CKD mice compared to the aorta of CTRL mice

OsteoSense staining showed intense calcification in the kidneys of CKD mice, while the signal intensity was low in the kidneys of CTRL mice. On bright field images, we detected tissue structural changes, atrophy, and fibrosis in the kidneys of CKD mice, which are characteristic

of renal failure. H&E staining showed tubular dilatation, and calcification was detectable by both alizarin red and von Kossa staining in kidneys from CKD mice.

According to our current knowledge, vascular calcification is an active process, during which osteochondrogenic differentiation occurs. Therefore, in our next experiment, we studied the changes in the expression of osteochondrogenic markers in CKD in aortic and kidney RNA samples from CTRL and CKD mice. We determined the mRNA levels of four transcription factors, Runx2, Sox9, Msx2, and Bmp2. In general, the mRNA expression of osteochondrogenic transcription factors increased in CKD compared to CTRL, both in the aorta and the kidney. However, we observed significant differences between tissues in terms of which transcription factor levels changed more significantly. In the aorta, the levels of Msx2 and Bmp2 increased the most, while in the kidney, the expression of Sox9 and Runx2 increased the most.

We then investigated whether CKD-induced calcification affects other vital organs. We first analyzed the heart, lungs, and liver. Whole-organ OsteoSense staining was detected in heart and lung samples from CKD mice.

We also examined the mRNA levels of osteochondrogenic markers in the heart, lungs, and liver of CTRL and CKD mice. We found increased Runx2 and Bmp2 levels in the heart and liver of CKD mice, while Sox9 mRNA levels were significantly increased in the lungs compared to CTRL mice.

We then examined calcification in the brain, eyes, and spleen of CTRL and CKD mice using OsteoSense staining. Microcalcification foci were detected in the brains of both CTRL and CKD mice, but the total fluorescence intensity of the brains did not show a statistically significant difference between the two groups. In some mice from both the CTRL and CKD groups, OsteoSense signal was observed in the retina, which appeared more frequently in the CKD group.

2. Study of the effect of DPD on calcification in a mouse model of CKD in vivo and in vitro on human VSMCs

Our research group has previously shown that hypoxia increases the calcification tendency of vascular smooth muscle cells through the activation of the HIF pathway. Our group has also demonstrated that in addition to hypoxia, hypoxia mimetics, which activate the HIF pathway under normoxic conditions, also have a pro-calcification effect. DPD is a PHD inhibitor

developed for the treatment of CKD-associated anemia, which activates the HIF pathway through the inhibition of PHD.

In the DPD study, 15 male C57BL/6 mice (8-12 weeks old) were randomly divided to three groups (n=5/group); CTRL, CKD and CKD+DPD (CKDD). CTRL mice were fed a normal rodent chow. CKD was induced as described in the previous chapter with a diet containing adenine and high phosphate. The dose of DPD was determined in preliminary experiments and the lowest dose that prevented anemia in CKD mice was chosen. Accordingly, DPD was administered orally in our experiment. DPD completely corrected the anemia induced by CKD, as shown by similar hemoglobin, red blood cell count and hematocrit values in CTRL and CKDD mice. Elevated plasma urea, creatinine, and phosphate levels indicated that renal function in CKDD mice was impaired to the same extent as in CKD mice. CKD treatment did not alter plasma calcium levels.

We examined the mRNA expression of some HIF target genes (glucose transporter 1 (Glut1), vascular endothelial growth factor A (VEGFA)) and ER stress markers (ATF4, CHOP, glucose-regulated protein 78 (GRP78)) in the kidney and aorta. We found that CKD increased the mRNA expression of Glut1, ATF4, CHOP and GRP78 in the kidney. DPD treatment enhanced both HIF and ER stress responses. In the aorta, CKDD treatment increased the mRNA expression of Glut1, VEGFA and CHOP threefold compared to CTRL.

We observed a significant increase in the protein expression of the ER stress markers ATF4 and CHOP in the kidneys of CKDD mice. We then examined the effect of DPD on aortic and renal calcification using OsteoSense staining in the previous experimental setup. OsteoSense staining showed significant calcification in the kidneys and aorta of CKD mice, which was further enhanced in CKDD mice treated with DPD. Runx2, Sox9, BMP2 and Msx2 mRNA levels were higher in the kidneys of CKD mice compared to CTRL mice. Sox9 and Msx2 mRNA levels were significantly higher in the kidneys of DPD-treated animals compared to CKD mice. In the aorta, CKD induced an increase in BMP2 mRNA expression compared to CTRL, while CKDD caused a significant increase in Sox9, BMP2 and Msx2 mRNA levels.

Overall, these results indicate that DPD treatment induces hypoxia response and ER stress, increases the expression of osteo-/chondrogenic markers, and promotes calcification in the kidney and aorta of CKD mice. DPD induces ER stress and promotes Pi-induced calcification of HAoSMCs. Given that ATF4 expression was significantly increased in the kidney by DPD

treatment and the key role of ATF4 in calcification is known, we first investigated the effect of DPD on ATF4 expression. We showed that DPD dose-dependently increased both ATF4 mRNA and protein expression in HAoSMCs.

The key role of ATF4 in calcification is known, so in our next experiment we investigated whether the pro-calcification effect of DPD is associated with increased expression of ATF4. We reduced ATF4 expression using siRNA technology, the effectiveness of which was verified by western blot. Knocking out ATF4 reduced the calcification-enhancing effect of DPD, which was demonstrated by Alizarin red staining and determination of extracellular matrix calcium and OCN levels.

Discussion

Calcification of the cardiovascular system is a common complication of chronic kidney disease, contributing to early cardiovascular mortality in CKD patients. In addition to the cardiovascular system, calcification of other soft tissues also occurs in CKD, the best known of which are renal calcification, which plays a role in the exacerbation of CKD, and calciphylaxis, in which small and medium-sized arterioles of the skin become calcified, resulting in the formation of non-healing ulcers on the lower extremities or trunk. Calcification of other organs and tissues is less well studied.

Our research group is interested in understanding the mechanism of CKD-associated calcification, one of the model systems of which is CKD C57BL/6 mice induced by adenine-containing diet. In recent years, OsteoSense staining has come into our field of vision, and has been used by a few research groups to quantify calcification. In these works, OsteoSense staining was performed in vitro on calcified VSMCs, aortas, and heart valves. However, OsteoSense staining can also be used in vivo and has been used in several works related to ossification processes. Our research group was the first to use OsteoSense staining to detect aortic calcification in vivo.

The in vivo application of OsteoSense raises the possibility of examining soft tissue calcification in any tissue. In the first part of my dissertation, I examined calcification in organs of control and CKD mice using OsteoSense staining. We showed that calcification in CKD mice affects the aorta, heart, kidney, lung, and liver. However, we did not find increased calcification in the brain, spleen, or eye.

OsteoSense staining was more sensitive in detecting calcification in the aorta than classical calcification staining methods, VKS and ARS staining. In addition to the aorta, we observed significant calcification in the kidneys of CKD mice compared to control mice, which is consistent with human data, according to which renal calcification is a frequent companion of CKD. Renal calcification begins in the early stages of CKD, its prevalence increases with disease progression, and in end-stage CKD it can be detected in more than half of patients. It is also known that renal calcification is not only a passive accompanying phenomenon, but also an etiopathogenetic factor in the progression of CKD. Renal calcification was also confirmed by VKS and ARS staining.

In addition to the aorta and kidney, CKD-associated calcification was found in the heart, lung, and liver, while no calcification was observed in organs from control mice. Calcification of the heart, especially of the aortic and mitral valves, is frequently associated with chronic kidney disease, especially in CKD patients undergoing hemodialysis. Valvular calcification occurs 10 to 20 years earlier in CKD patients than in the general population, contributing to the high incidence and prevalence of cardiovascular events even in young CKD patients.

Lung calcification is also common in CKD patients. Our results are consistent with previous studies in which the authors detected lung calcification in a mouse model of CKD induced by 5/6 nephrectomy.

In humans, liver calcification associated with CKD is very rare. The high sensitivity of OsteoSense staining allowed us to detect diffuse liver calcification in a mouse model of CKD for the first time. This method therefore provides an opportunity to study the currently unknown mechanism of this rare condition. The fact that the levels of some transcription factors that play a key role in osteochondrogenic differentiation were increased in tissues and organs calcified by CKD suggests active calcification mechanisms.

CKD affects both brain structure and function. In our work, we examined hydroxyapatite deposition in the brain and found no significant difference in brain calcification between CKD and control mice.

Regarding the eye, corneal, conjunctival, and retinal calcifications are frequently observed in chronic kidney disease patients undergoing hemodialysis. In previous work, our research group demonstrated corneal calcification in calcification-prone DBA/2J mice in an adenine-induced CKD model, and we found evidence that high phosphate and calcium levels trigger osteochondrogenic differentiation of corneal epithelial cells in a Runx2-dependent manner. In

the experiment presented here, we did not see corneal calcification in C57BL/6 mice, but we did see OsteoSense signal from the retinal part of the eye, which was more frequent in the CKD group than in the control group, although the difference was not significant.

Splenic calcification is rare, but a recent multicenter study reported splenic calcification in patients diagnosed with calcific uremic arteriolopathy. In the present study, we found that CKD did not induce splenic calcification in C57BL/6 mice. Consistent with OsteoSense staining, we did not find an increase in mRNA levels of osteogenic markers in the brain and spleen of CKD mice.

Overall, this study demonstrated that OsteoSense staining is a sensitive and effective method for detecting soft tissue calcification associated with chronic kidney disease. The imaging agent reliably identified multiple calcified organs and revealed tissue-specific patterns of ectopic calcification. These results are consistent with our previous knowledge that demonstrated the systemic nature of calcification in chronic kidney disease, particularly in vascular and renal tissues.

We found a correlation between OsteoSense positivity and increased expression of osteochondrogenic differentiation markers, and we found that osteochondrogenic markers are upregulated in a tissue-specific manner under CKD conditions. OsteoSense staining also detected calcification in organs such as the liver and heart, which are less frequently examined in standard CKD models. Due to its specificity, non-destructive nature, and ability to examine the entire organ, OsteoSense is a powerful tool for assessing ectopic calcification in vivo and ex vivo. It shows promise for future preclinical studies aimed at understanding the mechanisms of soft tissue calcification and developing anti-calcification therapies and evaluating their efficacy.

In the second part of my dissertation, I investigated the effect of DPD, a novel mechanism of action PHI used for the treatment of anemia associated with CKD, on calcification in an in vitro vascular smooth muscle cell model, as well as in the previously described adenine-induced CKD mouse model. DPD is a drug belonging to the PHI family, which stimulates the body's own erythropoietin production through the activation of the HIF pathway, enhances erythropoiesis and iron absorption, thereby correcting anemia. DPD has been used in Japan since 2020 and in the United States since 2023 for the treatment of anemia associated with CKD.

In our previous work, our group demonstrated that anemia develops in adenine-induced CKD mouse model, which can be successfully corrected with DPD. At the same time, we also demonstrated that the anemia-correcting dose of DPD enhances aortic calcification in CKD mice through the induction of the HIF-1 pathway. In my work, further investigating the pro-calcification mechanism of DPD, we found that DPD induces ER stress in vascular smooth muscle cells in vitro. By examining the different ER stress pathways, we found that DPD primarily activates the PERK branch of ER stress, which results in increased expression of ATF4 and CHOP. ATF4 plays a key role in the mechanism of vascular calcification, the most conclusive evidence of which is that smooth muscle cell-targeted ATF4 knock-out mice lack media calcification under CKD conditions. This is consistent with our results, according to which the calcification-enhancing effect of DPD is absent in the absence of ATF4.

Further investigating the mechanism of action of DPD on calcification, we found that DPD corrects the anemia in CKD mice, and the hemoglobin and hematocrit levels of DPD-treated mice remain at control levels. Consistent with our previous results, DPD increased aortic calcification in CKD mice. In this work, we also examined renal calcification, and similarly to the aorta, we found increased calcification in CKD mice treated with DPD. DPD increased the mRNA expression of osteochondrogenic markers (Sox9, Runx2, BMP2, Msx2) and HIF target genes (Glut-1, VEGFA) in both the aorta and kidney. Similar to our in vitro results, DPD increased the mRNA expression of ER stress markers ATF4, CHOP, and GRP78 in both the aorta and kidney.

In conclusion, our second study, in line with the literature, found that DPD is suitable for correcting CKD-associated anemia. However, concerns are raised that, in addition to its positive effect, DPD increases ER stress and aortic and renal calcification in CKD mice. Further studies are needed to determine whether the calcification-enhancing effect of DPD plays a role in the development of cardiovascular complications in CKD patients.

Summary

CKD is an increasing global public health problem, accompanied by high cardiovascular mortality. One of the major complications of CKD is vascular and soft tissue calcification, an active, cell-regulated process in which vascular smooth muscle cells undergo osteo/chondrogenic transdifferentiation.

One of the aims of our work was to establish a CKD mouse model induced by adenine and a high-phosphate diet, and to achieve non-invasive detection of calcification using the specific

fluorescent dye OsteoSense. Another goal was to elucidate the molecular mechanisms underlying the pro-calcific effects of DPD, employing the previously established CKD mouse model and the optimized OsteoSense-based detection method for calcification. Using *in vivo* imaging, we demonstrated that OsteoSense is suitable for detecting CKD-associated soft tissue calcification, particularly in the aorta, kidney, heart, lung, and liver. In the calcified tissues, we also observed increased expression of osteogenic markers.

Our findings on DPD showed that DPD effectively prevents the development of anemia in CKD mice. However, it also has adverse effects, as it enhances calcification. Using *in vitro* and *in vivo* approaches, we identified a central role for the transcription factor ATF4, a key component of the UPR, in mediating the calcification-promoting effect of DPD.

New findings

1. OsteoSense staining effectively identifies aortic calcification at an early stage, while conventional staining techniques barely detect calcification at this stage.
2. OsteoSense staining can detect renal, hepatic, pulmonary, and cardiac calcification in CKD mice.
3. CKD did not induce calcification in the spleen, brain, or eye.
4. OsteoSense positivity correlates with increased mRNA expression of osteochondrogenic transcription factors.
5. DPD corrects anemia in CKD mice.
6. DPD enhances aortic and renal calcification in CKD mice.
7. DPD increases the mRNA expression of HIF target genes, osteochondrogenic markers and ER stress markers in the aorta and kidney of CKD mice, and the protein expression of ATF4 and CHOP in the kidney of CKD mice.
8. DPD increases the expression of ER stress markers ATF4 and CHOP in vascular smooth muscle cells.
9. DPD enhances phosphate-induced calcification of vascular smooth muscle cells in an ATF4-dependent manner.



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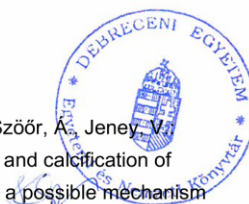
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List of publications related to the dissertation

1. **Lente, G.**, Tóth, A., Balogh, E., Csiki, D. M., Nagy, B. J., Szőör, Á., Jeney, V.: The OsteoSense Imaging Agent Identifies Organ-Specific Patterns of Soft Tissue Calcification in an Adenine-Induced Chronic Kidney Disease Mouse Model.
Int. J. Mol. Sci. 26 (17), 1-14, 2025.
DOI: <http://dx.doi.org/10.3390/ijms26178525>
IF: 4.9 (2024)
2. Tóth, A., **Lente, G.**, Csiki, D. M., Balogh, E., Szőör, Á., Nagy, B. J., Jeney, V.: Activation of PERK/eIF2 α /ATF4/CHOP branch of endoplasmic reticulum stress response and cooperation between HIF-1 α and ATF4 promotes Daprodustat-induced vascular calcification.
Front. Pharmacol. 15, 1-12, 2024.
DOI: <http://dx.doi.org/10.3389/fphar.2024.1399248>
IF: 4.8

List of other publications

3. Ababneh, H. M., Balogh, E., Csiki, D. M., **Lente, G.**, Fenyvesi, F., Tóth, A., Jeney, V.: High glucose promotes osteogenic differentiation of human lens epithelial cells through hypoxia-inducible factor (HIF) activation.
J. Cell. Physiol. 239 (5), 1-12, 2024.
DOI: <http://dx.doi.org/10.1002/jcp.31211>
IF: 4
4. Ababneh, H. M., Tóth, A., **Lente, G.**, Balogh, E., Csiki, D. M., Nagy, B. J., Szőör, Á., Jeney, V.: High phosphate and calcium induce osteoblastic phenotype switching and calcification of corneal epithelial cells in a Runx2-dependent and synergistic manner; a possible mechanism of chronic kidney disease-associated corneal calcification.
Biochim. Biophys. Acta. Mol. Basis Dis. 1870 (5), 1-20, 2024.
DOI: <http://dx.doi.org/10.1016/j.bbadis.2024.167171>
IF: 4.2





5. Csiki, D. M., Ababneh, H. M., Tóth, A., **Lente, G.**, Szőör, Á., Tóth, A., Fillér, C., Juhász, T., Nagy, B. J., Balogh, E., Jeney, V.: Hypoxia-inducible factor activation promotes osteogenic transition of valve interstitial cells and accelerates aortic valve calcification in a mice model of chronic kidney disease.
Front. Cardiovasc. Med. 10, 1-15, 2023.
DOI: <http://dx.doi.org/10.3389/fcvm.2023.1168339>
IF: 2.8
6. Tóth, A., Csiki, D. M., Nagy, B. J., Balogh, E., **Lente, G.**, Ababneh, H. M., Szőör, Á., Jeney, V.: Daprodustat Accelerates High Phosphate-Induced Calcification Through the Activation of HIF-1 Signaling.
Front. Pharmacol. 13, 1-12, 2022.
DOI: <http://dx.doi.org/10.3389/fphar.2022.798053>
IF: 5.6
7. Sári, Z., Mikó, E., Kovács, T., Jankó, L., Csonka, T., **Lente, G.**, Sebő, É., Tóth, J., Tóth, D., Árkosy, P., Boratkó, A., Ujlaki, G., Török, M., Kovács, I., Szabó, J., Kiss, B. K., Méhes, G., Goedert, J. J., Bai, P.: Indolepropionic Acid, a Metabolite of the Microbiome, Has Cytostatic Properties in Breast Cancer by Activating AHR and PXR Receptors and Inducing Oxidative Stress.
Cancers (Basel). 12 (9), 1-27, 2020.
DOI: <http://dx.doi.org/10.3390/cancers12092411>
IF: 6.639
8. Kovács, T., Mikó, E., Vida, A., Sebő, É., Tóth, J., Csonka, T., Boratkó, A., Ujlaki, G., **Lente, G.**, Kovács, P., Tóth, D., Árkosy, P., Kiss, B. K., Méhes, G., Goedert, J. J., Bai, P.: Cadaverine, a metabolite of the microbiome, reduces breast cancer aggressiveness through trace amino acid receptors.
Sci Rep. 9 (1), 1-14, 2019.
DOI: <http://dx.doi.org/10.1038/s41598-018-37664-7>
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